32. Ulusal
Çocuk ve Ergen
Ruh Sağlığı ve Hastalıkları
Kongresi

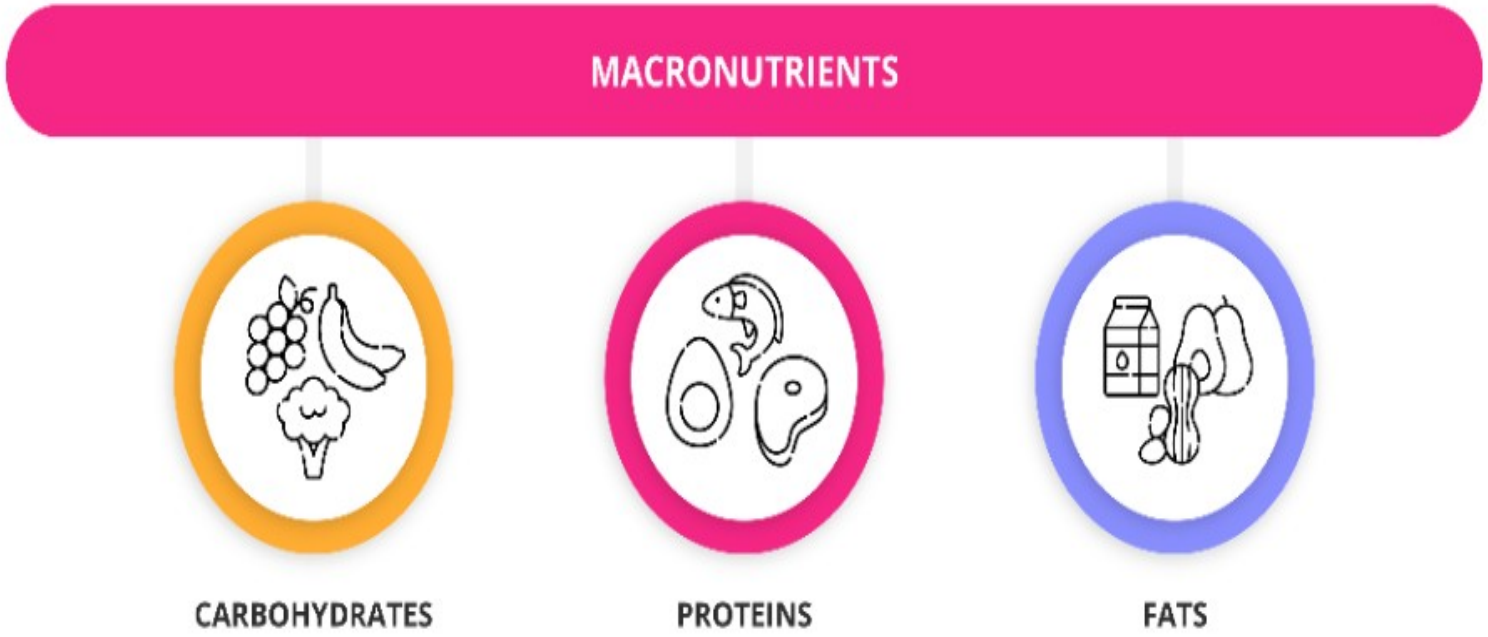
MİKROBESİNLER
(Vitamin-Mineraller)

Doç. Dr. Gülen GÜLER AKSU

Mersin Üniversitesi Çocuk Ve Ergen Ruh Sağlığı Ve Hastalıkları AD

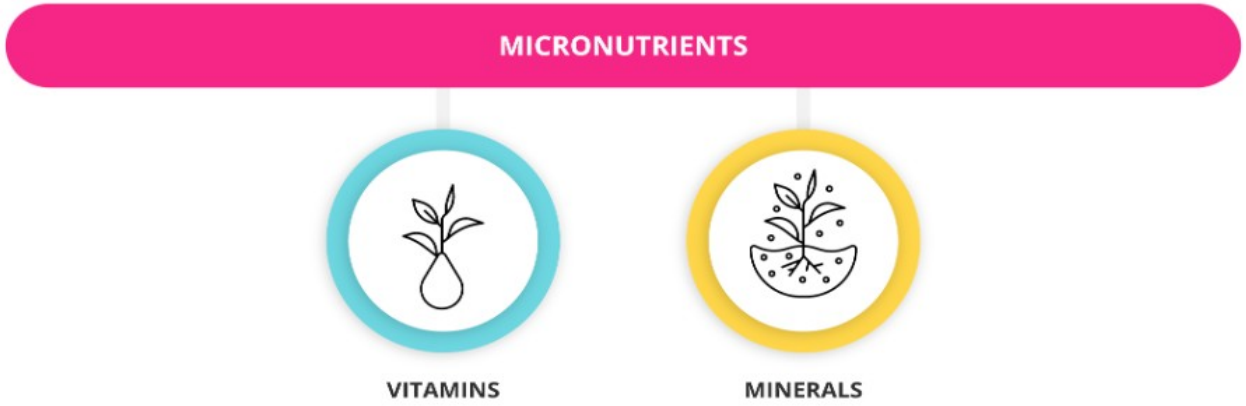
SUNUM PLANI

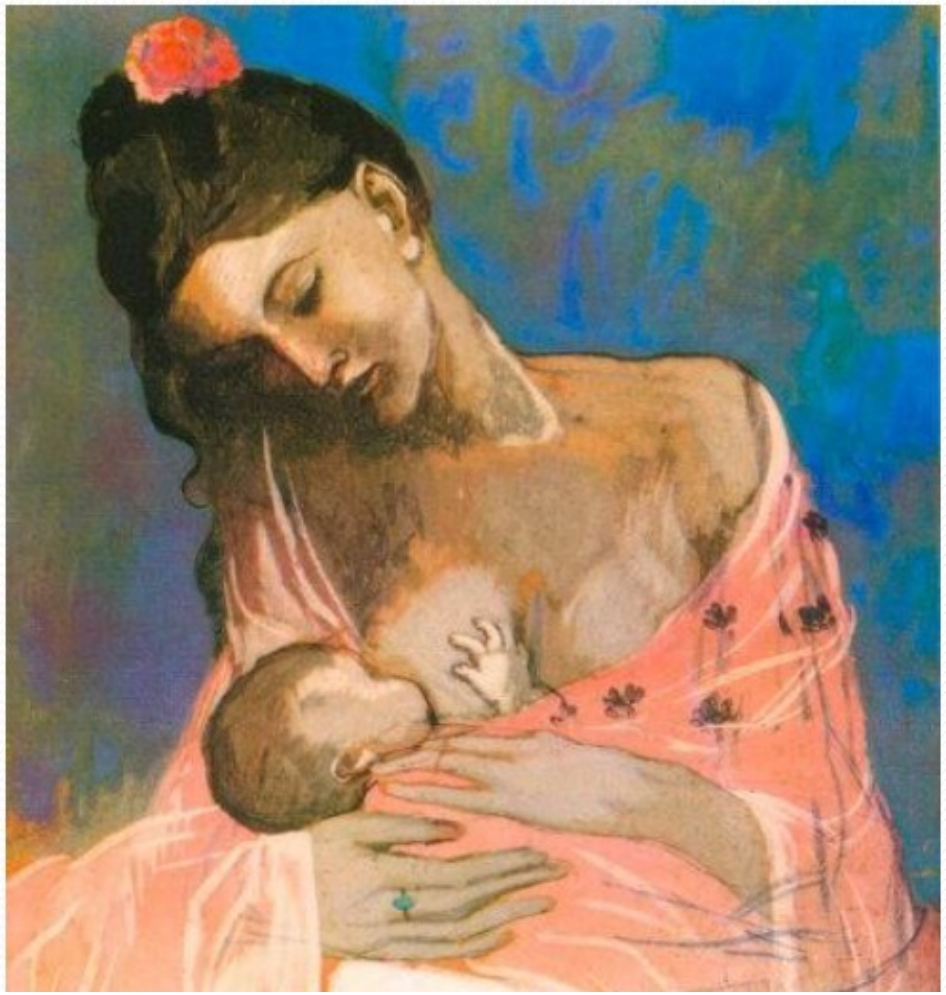
- Makrobesinler-mikrobesinler nedir?
- Erken dönem beyin gelişiminde mikrobesinlerin önemi nedir?
- Mikrobesinler ve ruh sağlığı üzerindeki etkileri
- Mikrobesinler ve ilişkili ruhsal sorunlar
- Vitaminler ve mineraller ile ilgili güncel çalışmalar



We need macronutrients to help with energy and we need micronutrients to help our body be healthy and digest those macronutrients.[6]

Doctor Donald Hensrud, the Mayo Clinic



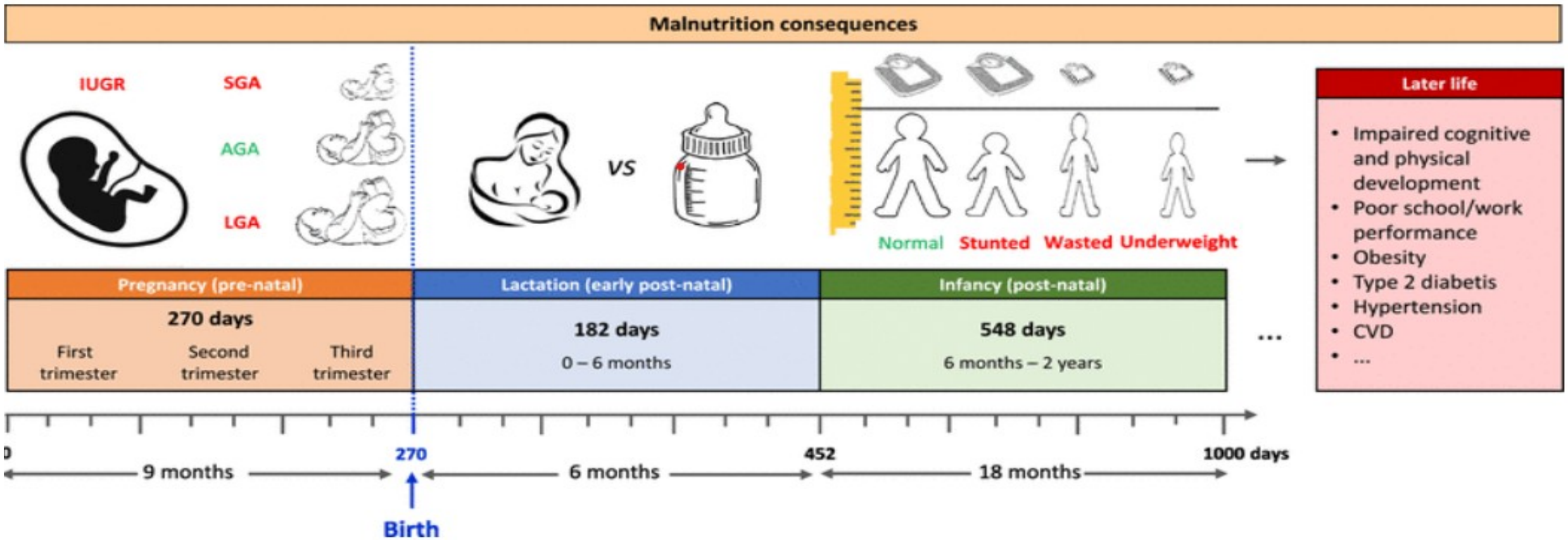


Hayata sağlıklı başlamak ve devam etmek önemli

Why First 1000 Days are Important ?

FIRST 1000 DAYS

nutrition now, matters forever



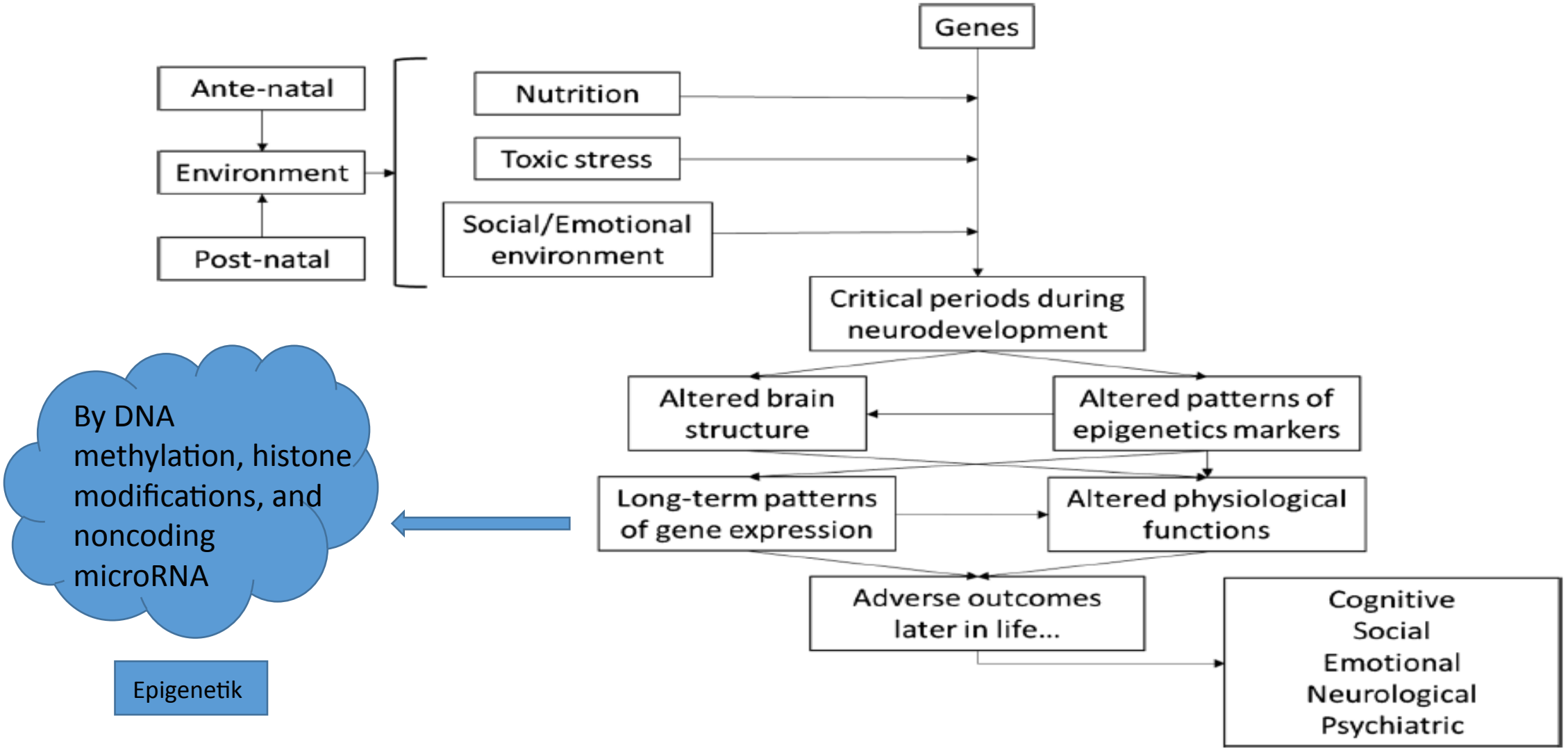


Fig. 1 Interactions between genes and environment shape human development. Early life nutrition (prenatal and neonatal) represents a fundamental environmental factor that can profoundly affect brain development. Early life malnutrition, during critical periods of neurodevelopment, can create an altered brain structure and induce altered patterns of epigenetic markers, leading to brief- and long-term adverse health consequences with respect to cognitive, social, emotional, neurological, and psychiatric performances

En çok satılan ilaçlar

Dünya

Türkiye

1. Kalp-damar	% 19.3	1. Antibiyotik	% 19.0
2. Santral SS	% 15.8	2. Ağrı kesici	% 12.0
3. Metabolik	% 15.3	3. Romatizma	% 11.0
4. Antibiyotik	% 9.9	4. Soğuk algın.	% 8.6
5. Solunum S.	% 9.3	5. Vitamin	% 7.3

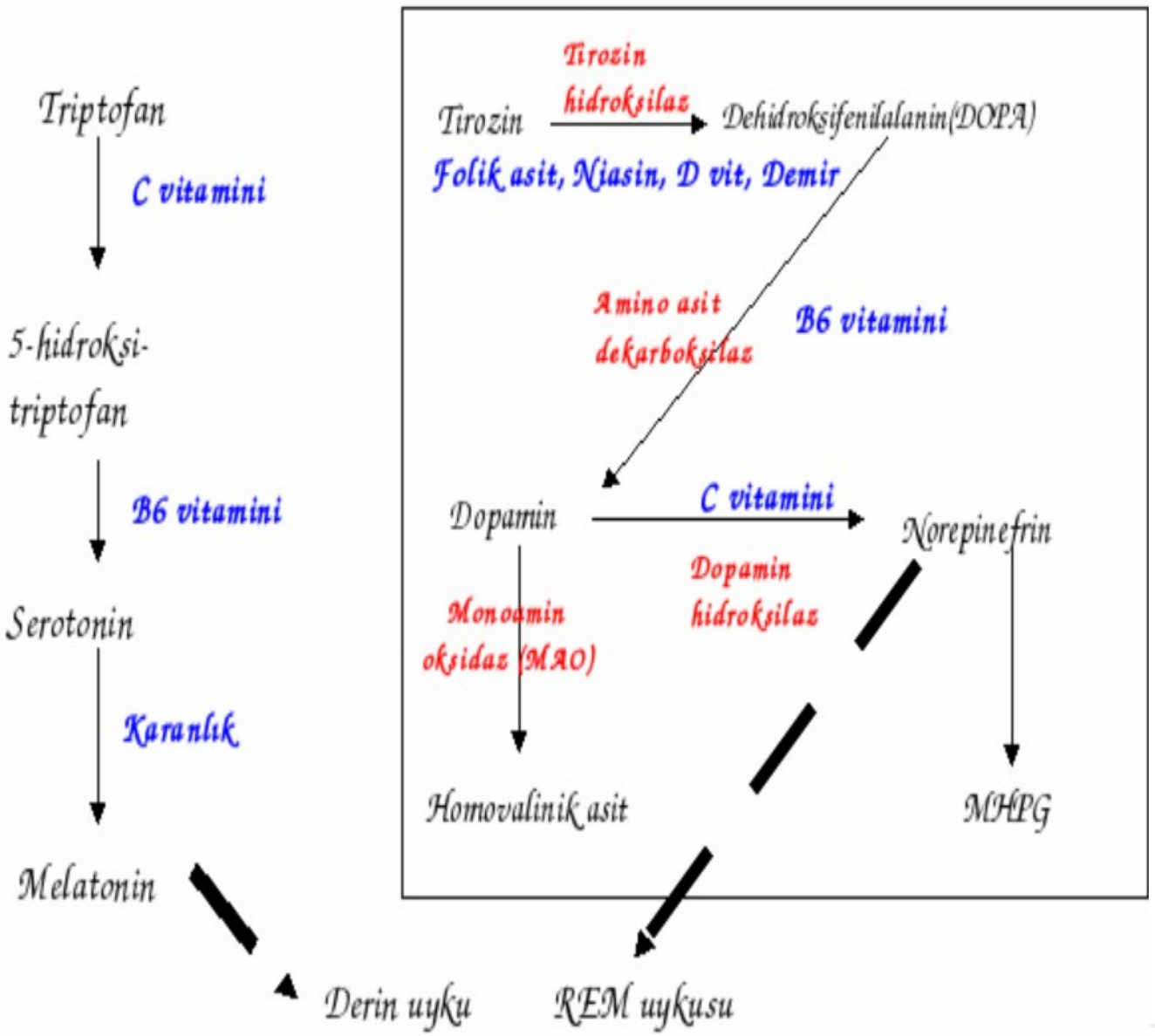
Vitaminlerin keşif tarihleri ve kaynakları

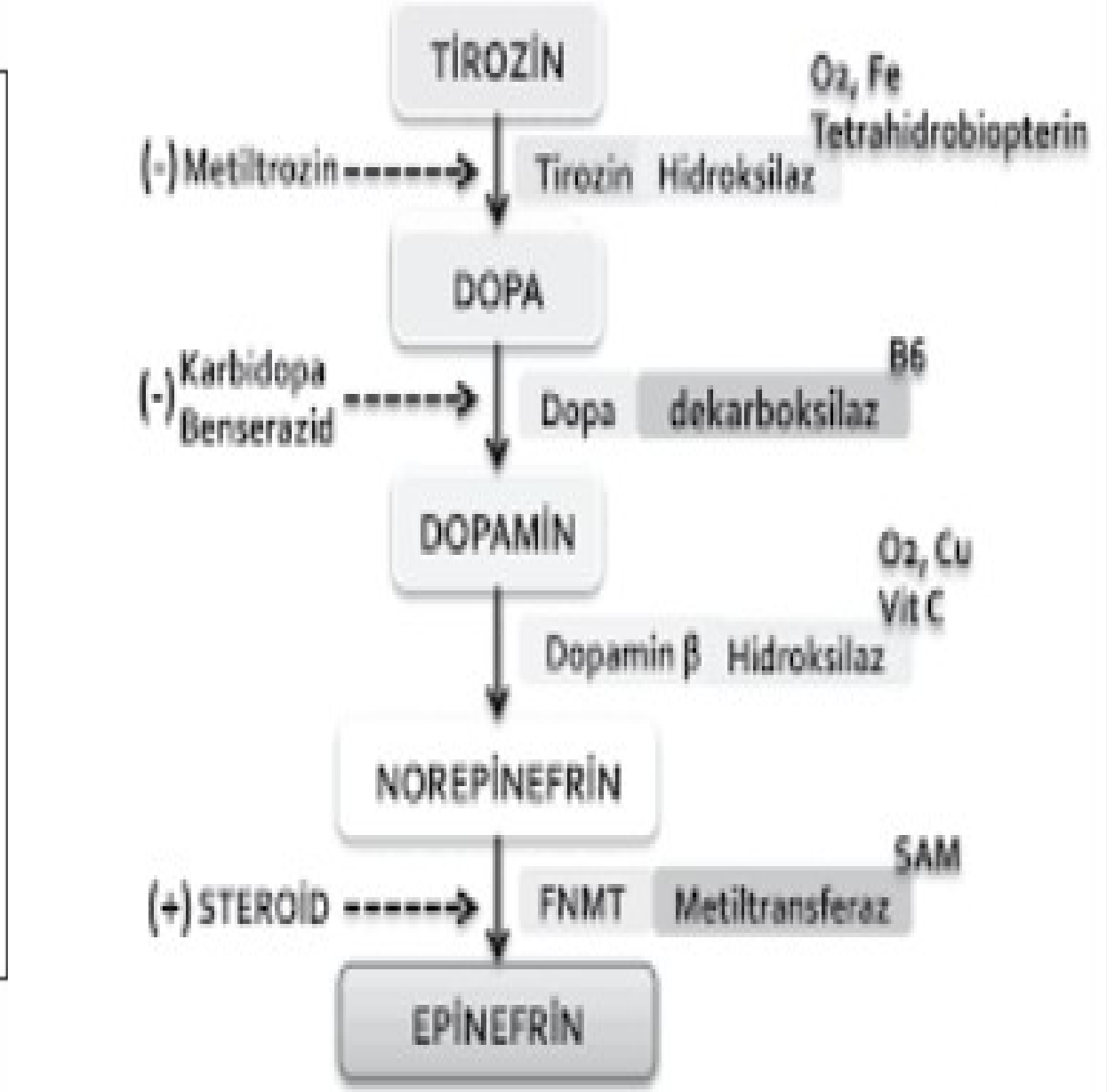
YIL	Vitamin		Kaynak
1909	Vitamin A	Retinol	Cod karaciğer yağı
1912	Vitamin B1	Tiamin	Pirinç kepeği
1912	Vitamin C	Askorbik asit	Limon
1918	Vitamin D	Kalsiferol	Cod karaciğer yağı
1920	Vitamin B2	Riboflavin	Yumurta
1922	Vitamin E	Tokoferol	Buğday ruşeymi yağı kozmetikler ve karaciğer
1926	Vitamin B12	Siyanokobalamin	Karaciğer
1929	Vitamin K	Fillakinon	Alfaalfa
1931	Vitamin B5	Pantotenik asit	Karaciğer
1931	Vitamin B7	Biotin	Karaciğer
1934	Vitamin B6	Piridoksin	Pirinç kepeği
1936	Vitamin B3	Niasin	Karaciğer
1941	Vitamin B9	Folik asit	Karaciğer

Mineraller

- Sodyum (Na)
- Potasyum (K)
- Klor (Cl)
- Magnezyum (Mg)
- Kalsiyum (Ca)
- Fosfor (P)
- Bakır (Cu)
- Demir (Fe)
- Çinko (Zn)
- Kobalt (Co)
- Molibden (Mo)
- Manganez (Mn)

- Kadmiyum (Cd)
- Lityum (Li)
- Selenyum (Se)
- Krom (Cr)
- Nikel (Ni)
- Vanadyum (V)
- Arsenik (As)
- Silisyum (Si)
- Bor (B)
- Kükürt (S)
- İyot (I)
- Flüor (F)

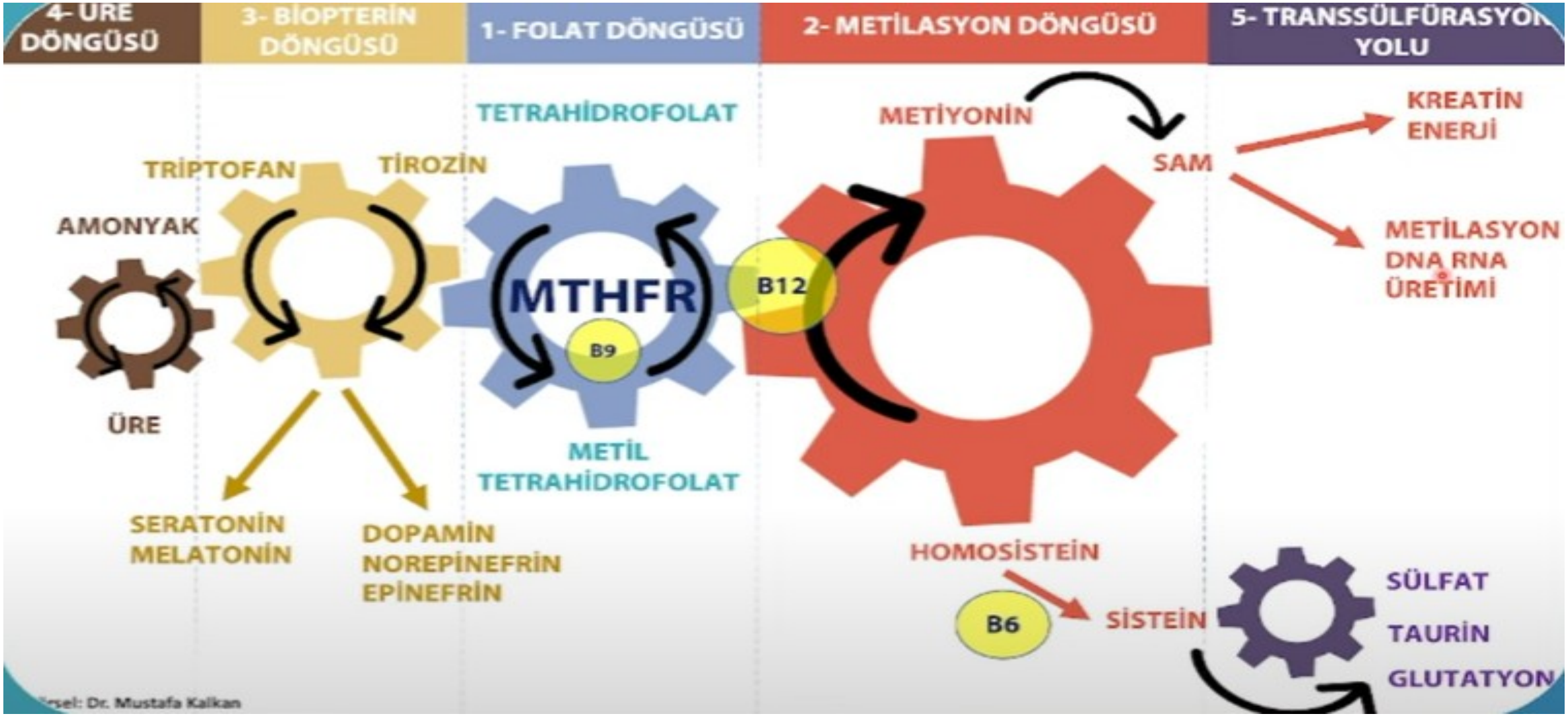




- Serotonin, dopamin, noradrenalin sentezini etkileyen vitaminler

VİTAMİN B

B1 VİTAMİNİ
-Tiamin
B2 VİTAMİNİ
-Riboflavin
B3 VİTAMİNİ
-Niasin
B5 VİTAMİNİ
-Pantotenik asit
B6 VİTAMİNİ
-Piridoksin
B7 VİTAMİNİ
-Biyotin
B9 VİTAMİNİ
-Folik asit
B12 VİTAMİNİ
-Kobalamin


4- ÜRE DÖNGÜSÜ
3- BİOPTERİN DÖNGÜSÜ
1- FOLAT DÖNGÜSÜ
2- METİLASYON DÖNGÜSÜ
5- TRANSSÜLFÜRASYON YOLU
TETRAHİDROFOLAT
METİYONİN
SAM
KREATİN
ENERJİ
METİLASYON
DNA RNA
ÜRETİMİ
TRİPTOFAN
TİROZİN
AMONYAK
MTHFR
B12
B9
ÜRE
METİL
TETRAHİDROFOLAT
SERATONİN
MELATONİN
DOPAMİN
NOREPİNEFRİN
EPİNEFRİN
HOMOSİSTEİN
B6
SİSTEİN
SÜLFAT
TAURİN
GLUTATYON

B vitamini ile ilişkili psikiyatrik bozukluklar

- Depresyon
- Anksiyete bozuklukları
- Psikoz
- Kognitif sorunlar
- Delirium

(Sahu P, et al. Vitam Horm. 2022)

Low intake of B-vitamins is associated with poor adolescent mental health and behaviour

Carly E. Herbison [a], Siobhan Hickling [a,b], Karina L. Allen [a,c], Therese A. O'Sullivan [a,d], Monique Robinson [a,c], Alexandra P. Bremner [b], Rae-Chi Huang [e,f], Lawrence J. Beilin [e], Trevor A. Mori [e], Wendy H. Oddy [a,*]

- The Western Australian Pregnancy Cohort (Raine) Study
- 2868 çocuk doğumu itibari ile 17 yıllık takip
- B vitamini alımının hesaplandığı yeme sıklığı anketi, YSR (internalizasyon, eksternalizasyon ve total skorlar)
- B1, B2,B3, B5,B6 ve folat yetersizliği, yüksek eksternalizasyon skorları ile ilişkili,
- B6 ve folat eksikliği yüksek internalizasyon skorları ile ilişkili saptanmış

C.E. Herbison et al. / Preventive Medicine (2012)

Review

A Systematic Review and Meta-Analysis of B Vitamin Supplementation on Depressive Symptoms, Anxiety, and Stress: Effects on Healthy and 'At-Risk' Individuals

Abstract: A systematic review and meta-analysis was undertaken to examine and quantify the effects of B vitamin supplementation on mood in both healthy and 'at-risk' populations. A systematic search identified all available randomised controlled trials (RCTs) of daily supplementation with ≥3 B group vitamins with an intervention period of at least four weeks. Random effects models for a standardized mean difference were used to test for overall effect. Heterogeneity was tested using the I^2 statistic. Eighteen articles (16 trials, 2015 participants) were included, of which 12 were eligible for meta-analysis. Eleven of the 18 articles reported a positive effect for B vitamins over a placebo for overall mood or a facet of mood. Of the eight studies in 'at-risk' cohorts, five found a significant benefit to mood. Regarding individual facets of mood, B vitamin supplementation benefited stress ($n = 958$, SMD = 0.23, 95% CI = 0.02, 0.45, $p = 0.03$). A benefit to depressive symptoms did not reach significance ($n = 568$, SMD = 0.15, 95% CI = −0.01, 0.32, $p = 0.07$), and there was no effect on anxiety ($n = 562$, SMD = 0.03, 95% CI = −0.13, 0.20, $p = 0.71$). The review provides evidence for the benefit of B vitamin supplementation in healthy and at-risk populations for stress, but not for depressive symptoms or anxiety. B vitamin supplementation may particularly benefit populations who are at risk due to (1) poor nutrient status or (2) poor mood status.

Young LM,et al. Nutrients 2019

Associations of dietary vitamin B1, vitamin B2, vitamin B6, and vitamin B12 with the risk of depression: a systematic review and meta-analysis

Yanjun Wu*, Liming Zhang*, Suyun Li, and Dongfeng Zhang

Population	Children, adolescents, and adults without regard to sex or race
Intervention or exposure	Dietary intake of vitamin B1, vitamin B2, vitamin B6, and vitamin B12 (with or without supplements)
Comparison	RRs and 95% CIs in the highest intake category compared with the lowest intake category[Reference]
Outcome	Depression
Study design	Observational study design

B1 ve depresyon

- 5 makale'nin 4 ünde B1 ve depresyon arasında bir ilişki yoktu. Bir çalışmada B1 yetersizliği ile depresyon arasında bir ilişki
- RR:0.69

Wu Y, et al. Nutr Rev. 2022

Associations of dietary vitamin B1, vitamin B2, vitamin B6, and vitamin B12 with the risk of depression: a systematic review and meta-analysis

Yanjun Wu*, Liming Zhang*, Suyun Li, and Dongfeng Zhang

B2 ve depresyon

- 8 çalışmadan 7'sinde B2 ile depresyon arasında bir ilişki yok, bir çalışmada yetersizliği ile ilişkili
- RR: 0.77

B6 ve depresyon

- 14 çalışmanın 9 unda ilişki yok diğer 5 çalışmada B6 yeteriijliği ile ilişkili
- RR:0.81

B12 ve depresyon

- 12 çalışmanın 10 unda ilişki yok, diğer 2 çalışmada B12 yetersizliği ile ilişkili
- RR: 0.86

Wu Y, et al. Nutr Rev. 2022

Vitamin B-12 status in infancy is positively associated with development and cognitive functioning 5 y later in Nepalese children[1]

*Ingrid Kvestad,[2] Mari Hysing,[2] Merina Shrestha,[3] Manjeswori Ulak,[3] Andrew L Thorne-Lyman,[4–6] Sigrun Henjum,[7] Per M Ueland,[8,10] Øyvind Midttun,[11] Wafaie Fawzi,[6] Ram K Chandyo,[3] Prakash S Shrestha,[3] and Tor A Strand[9,12]**

- 320 çocukta (2-12 ay) B-12 vitamini durumu ile 5 yıl sonraki gelişim ve bilişsel işlevsellik arasındaki ilişki
- Bebeklikte B-12 vit, homosistein (tHcy) ve metilmalonik asit (MMA) değerlendirildi
- Düşük B12, yüksek MMA ve tHcy, 5 yaşta problem çözme puanlarında düşüş ve kötü nörogelişimle ilişkili

Kvetad I, et al. Am J Clin Nutr 2017;105:1122–31.

Prenatal folate, homocysteine and vitamin B_{12} levels and child brain volumes, cognitive development and psychological functioning: the Generation R Study

- Prospektif kohort çalışması, 256 Hollandalı çocuk (6-8 yaş) beyin taramaları MR ile yapılmış
- 62 çocuğun annesinde gebeliğin erken döneminde folat yetersizliği (<8 nmol/l)+
- Düşük prenatal folat seviyesi, düşük total beyin volümü ile dil gelişimimde düşük performans ile ilişkili,
- Yüksek homosistesi seviyesi (>9·1 µmol/l) de dil gelişimimde düşük performans ile ilişkili ve IQ larında önemli derecede düşüş
- B12 ve folat için zeka ile anlamlı ilişki yok.
- Psikolojik sorunlarla ilişki saptanmamış.

Ars CL, et al, *British Journal of Nutrition 2016*

Maternal serum Vitamin B12 and offspring attention-deficit/ hyperactivity disorder (ADHD)

Andre Sourander[1,2,3] · Sanju Silwal[1] · Subina Upadhyaya[1] · Heljä-Marja Surcel[4,5] · Susanna Hinkka-Yli-Salomäki[1] · Ian W. McKeague[6] · Keely Cheslack-Postava[7] · Alan S. Brown[7,8]

- 1026 olgu, eşleştirilmiş kontrol
- 1. ve erken 2. trimestrer maternal B12 düzeyleri karşılaştırılmış
- Düşük maternal B12, çocukta ADHD ile ilişkili değildi.
- En düşük B12 seviyelerinde bile anlamlı ilişki yoktu
- Maternal B12 başka bozukluklarla ilişkilendirilse de ADHD ile bağlantı saptanmadı

Sourander A, et al. European Child & Adolescent Psychiatry, 2021

Is High Folic Acid Intake a Risk Factor for Autism?—A Review

Darrell Wiens [1,*] and M. Catherine DeSoto [2]

Table 1. Five important empirical findings related to Folic Acid supplementation.

FA Supplementation Actual Intakes are Higher than Were Projected When Supplementation Was Instituted.	Quinlivan & Gregory, 2003 [29]
Unmetabolized FA occurs in cord blood, and in a dose dependent manner in serum when FA supplementation is more than about 200 µg/d.	Sweeney at al., 2006 [25]; Kalmbach et al., 2008 [24]; Troen et al., 2006 [27]; Obeid et al., 2010 [28]
Evidence from rodent studies showed that FA exposure during gestation caused changes in gene expression and anxiety, and hyperactivity in offspring. Exposure to higher-dose FA diet during gestation caused dysregulation of expression of many genes, including neuro-developmental genes, and epigenomic changes.	Barua et al., 2014 [38]; 2015 [39], 2016 [40]
Some women exceed recommended levels of FA during pregnancy.	Hoyo et al., 2011 [48]; Raghavan et al., 2016 [15], 2017 [49]
Folic acid can inhibit neurite extension, growth cone activity and synaptogenesis.	Wiens et al., 2016 [41]

Is High Folic Acid Intake a Risk Factor for Autism?—A Review

Darrell Wiens [1,*] and M. Catherine DeSoto [2]

- **Suren et al 201**: prospective nationwide cohort study
  OR:0.61
- **Schmidt et al 2012**: A large, well-vetted database

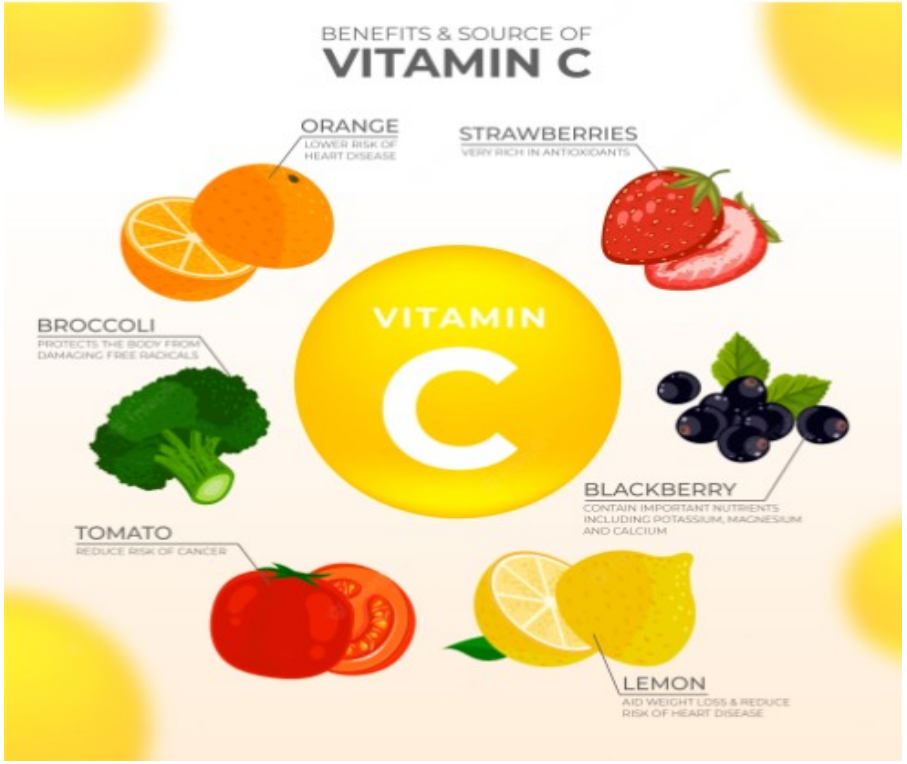
FA ASD için koruyucu

- **DeSoto and Hitlan 2012**: database, case-control design
  OR: 2.34
- **Raghavan et al 2016**: prospective birth cohort
- **Raghavan et al 2017**: prospective birth cohort

FA ASD için riskli

VİTAMİN C

- Kollojen, karnitin ve nörotransmitter sentezinde rol alan suda çözünen bir vitamin
- Antikoksidan ve immun sistem destekler
- Çalışmalar C vitamininin **nöroprotektif** etkilerinden bahseder



VİTAMİN C

- Depresyon
- Kognitif bozulma

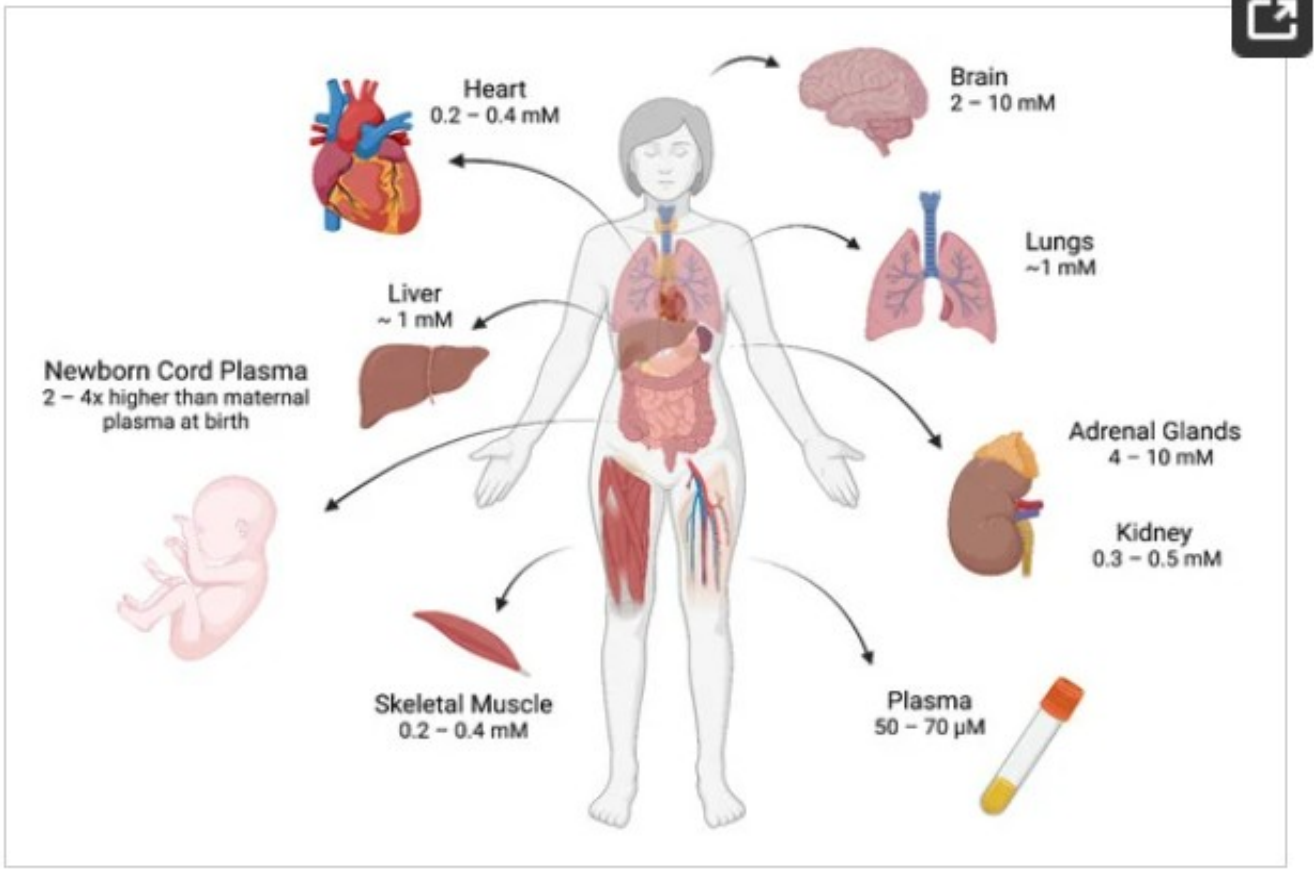


Figure 1. Tissue Distribution of Vitamin C. Vitamin C is present at different concentration
Notably, the concentration of vitamin C is particularly high in the brain and adrenal
newborn retaining higher plasma concentrations of vitamin C that its mother at the tim
observations highlight the importance of understanding the role of vitamin C during neuro
created with **Biorender.com** using published data [19].

Current Medical Science
DOI https://doi.org/10.1007/s11596-018-1840-2 38(1):1-10,2018

Preventive and Therapeutic Potential of Vitamin C in Mental Disorders*

Summary: In this review, we summarize the involvement of vitamin C in mental disorders by presenting available evidence on its pharmacological effects in animal models as well as in clinical studies. Vitamin C, especially its reduced form, has gained interest for its multiple functions in various tissues and organs, including central nervous system (CNS). Vitamin C protects the neuron against oxidative stress, alleviates inflammation, regulates the neurotransmission, affects neuronal development and controls epigenetic function. All of these processes are closely associated with psychopathology. In the past few decades, scientists have revealed that the deficiency of vitamin C may lead to motor deficit, cognitive impairment and aberrant behaviors, whereas supplement of vitamin C has a potential preventive and therapeutic effect on mental illness, such as major depressive disorder (MDD), schizophrenia, anxiety and Alzheimer's disease (AD). Although several studies support a possible role of vitamin C against mental disorders, more researches are essential to accelerate the knowledge and investigate the mechanism in this field.

HAN Q, et al. Current Medical Science, 2018

VİTAMİN D

- Oksidatif stresten koruyucu
- DNA stabilizasyonu
- Antiinflamatuar etki
- Otoimmüniteyi azalttığı ve
- Nörotrofinleri (NGF, NT-3, NT-4, GDNF) yukarı regüle ettiği bildirilmektedir.
- 1.25(OH)2D3 dopaminerjik nöronların farklılaşmasını ve olgunlaşmasını modüle eder, serotonin konsantrasyonlarını triptofan hidroksilazı indiksüyon yoluyla etkileyebilir.

(Cannell & Grant, 2013; Cui X, et al 2015; Garcion E et al. 2002).

25(OH)Vitamin D Düzeyi

- Institute of Medicine (IOM) 2010
  - Eksiklik : < 30 nmol/L (<12 ng/ml)
  - Yetersizlik : 30-50 nmol/L (12-20 ng/ml)
  - Normal : > 50 nmol/L (>20 ng/ml)

(>20 ng/ml toplumun en az %97.5'unun gereksinimini karşılar)

Çocuklarda D Vitamini Desteği Önerisi

İlk yaşta günde 400 IU
İlk yaştan sonra günde 600 IU

Amerikan Pediatri Akademisi ve Beslenme Komitesi
(IOM, Dietary Reference Intakes for Calcium and Vitamin D, NAP, 2011)

D vitamini ile ilişkili psikiyatrik bozukluklar

- Çocukluk çağı nöropsikiyatrik bozuklukları (DEHB, otizm)
- Depresyon
- Anksiyete, OKB
- Şizofreni
- Delirium

- (Berk et al., 2007; Cannell &Grant, 2013; Sharif, Madani, Tabatabaei, & Tabatabaee,2015).

Vitamin D levels in children and adolescents with attention-deficit hyperactivity disorder (ADHD): a meta-analysis

Study or Subgroup	ADHD children Mean	SD	Total	non-ADHD children Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Bala 2016	19.49	8.53	34	28.73	9.04	27	9.7%	-1.04 [-1.58, -0.50]
Bener 2014	16.81	7.84	630	22.18	9	630	15.3%	-0.64 [-0.75, -0.52]
Garipardic 2017	18.5	8.53	36	29.42	9.07	25	9.4%	-1.23 [-1.79, -0.67]
Goksugur 2014	20.9	19.4	60	34.9	15.4	30	10.9%	-0.76 [-1.22, -0.31]
Kamal 2014	16.6	7.8	1331	23.5	9	1331	15.5%	-0.82 [-0.90, -0.74]
Meyer 2016	16.42	8.21	430	17.94	11.21	6492	15.4%	-0.14 [-0.24, -0.04]
Shang-Guan 2015	17	7	97	23	8	97	13.3%	-0.80 [-1.09, -0.50]
Sharif 2015	19.11	10.1	37	28.67	13.76	37	10.6%	-0.78 [-1.26, -0.31]
Total (95% CI)			**2655**			**8669**	**100.0%**	**-0.73 [-1.00, -0.46]**

Heterogeneity: $Tau^2 = 0.12$; $Chi^2 = 126.22$, $df = 7$ ($P < 0.00001$); $I^2 = 94\%$

Test for overall effect: $Z = 5.31$ ($P < 0.00001$)

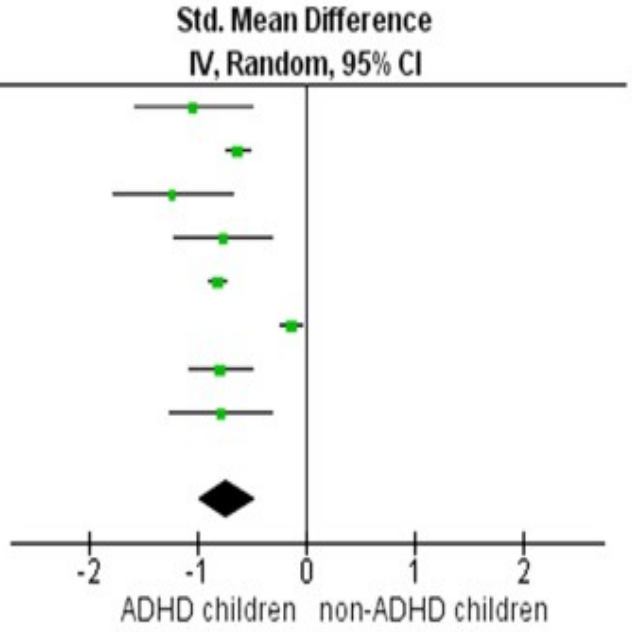


Fig. 2 Forest plot of the serum vitamin D concentration in ADHD and healthy controls

- 8 çalışma toplam 11324 çocuk
- 2655 çocuk DEHB tanılı

Kotsi E, et al. *ADHD Atten Def Hyp Disord 2022*

The Effect of Vitamin D Supplementation on Attention-Deficit/Hyperactivity Disorder: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

- 4 RCT, 256 çocuk
- DEHB'de metilfenitat tedavisine Vitamin D takviyesi eklendiğinde
- DEHB total, de, hp ve davranış puanlarında küçük ama anlamlı iyileşme, karşıt olma puanlarında iyileşme yoktu.

- Literatürde düşük ve çok düşük güçte kanıtlar söz konusu olması nedeniyle iyileşmenin sınırlı olduğu sonucuna varılmış.

Gan J, et al J Child Adolesc Psychopharmacol. 2019

Review

The Association between Vitamin D Status and Autism Spectrum Disorder (ASD): A Systematic Review and Meta-Analysis

Zuqun Wang [1,2], Rui Ding [1,2] and Juan Wang [1,2,*]

Abstract: The association between vitamin D status and autism spectrum disorder (ASD) is well-investigated but remains to be elucidated. We quantitatively combined relevant studies to estimate whether vitamin D status was related to ASD in this work. PubMed, EMBASE, Web of Science, and the Cochrane Library were searched to include eligible studies. A random-effects model was applied to pool overall estimates of vitamin D concentration or odds ratio (OR) for ASD. In total, 34 publications involving 20,580 participants were identified in this present study. Meta-analysis of 24 case–control studies demonstrated that children and adolescents with ASD had significantly lower vitamin D concentration than that of the control group (mean difference (MD): −7.46 ng/mL, 95% confidence interval (CI): −10.26; −4.66 ng/mL, $p < 0.0001$, $I^2 = 98\%$). Quantitative integration of 10 case–control studies reporting OR revealed that lower vitamin D was associated with higher risk of ASD (OR: 5.23, 95% CI: 3.13; 8.73, $p < 0.0001$, $I^2 = 78.2\%$). Analysis of 15 case–control studies barring data from previous meta-analysis reached a similar result with that of the meta-analysis of 24 case–control studies (MD: −6.2, 95% CI: −9.62; −2.78, $p = 0.0004$, $I^2 = 96.8\%$), which confirmed the association. Furthermore, meta-analysis of maternal and neonatal vitamin D showed a trend of decreased early-life vitamin D concentration in the ASD group (MD: −3.15, 95% CI: −6.57; 0.26, $p = 0.07$, $I^2 = 99\%$). Meta-analysis of prospective studies suggested that children with reduced maternal or neonatal vitamin D had 54% higher likelihood of developing ASD (OR: 1.54, 95% CI: 1.12; 2.10, $p = 0.0071$, $I^2 = 81.2\%$). These analyses indicated that vitamin D status was related to the risk of ASD. The detection and appropriate intervention of vitamin D deficiency in ASD patients and pregnant and lactating women have clinical and public significance.

- 20580 kişiden oluşan 34 yayın
- 24 vaka –kontrol çalş. ASD'li çocuklarda daha düşük D vit düzeyleri olduğu,
- OR bildiren 10 vaka-kontrol çalş. D vit düşük olanların **5.23 kat** daha fazla ASD olduğu,
- ASD grubunda maternal veya neonatal D vit konsantrasyonları istatistiksel anlamlı düzeyde daha az olduğu,
- Azalmış maternal veya neonatal vit D düzeyleri olanların ASD geliştirme olasılığının **%54** daha yüksek olduğunu gösterdi.

Wang Z, et al. Nutrients 2021, 13, 86

Systematic Review

The Influence of Vitamin D Intake and Status on Mental Health in Children: A Systematic Review

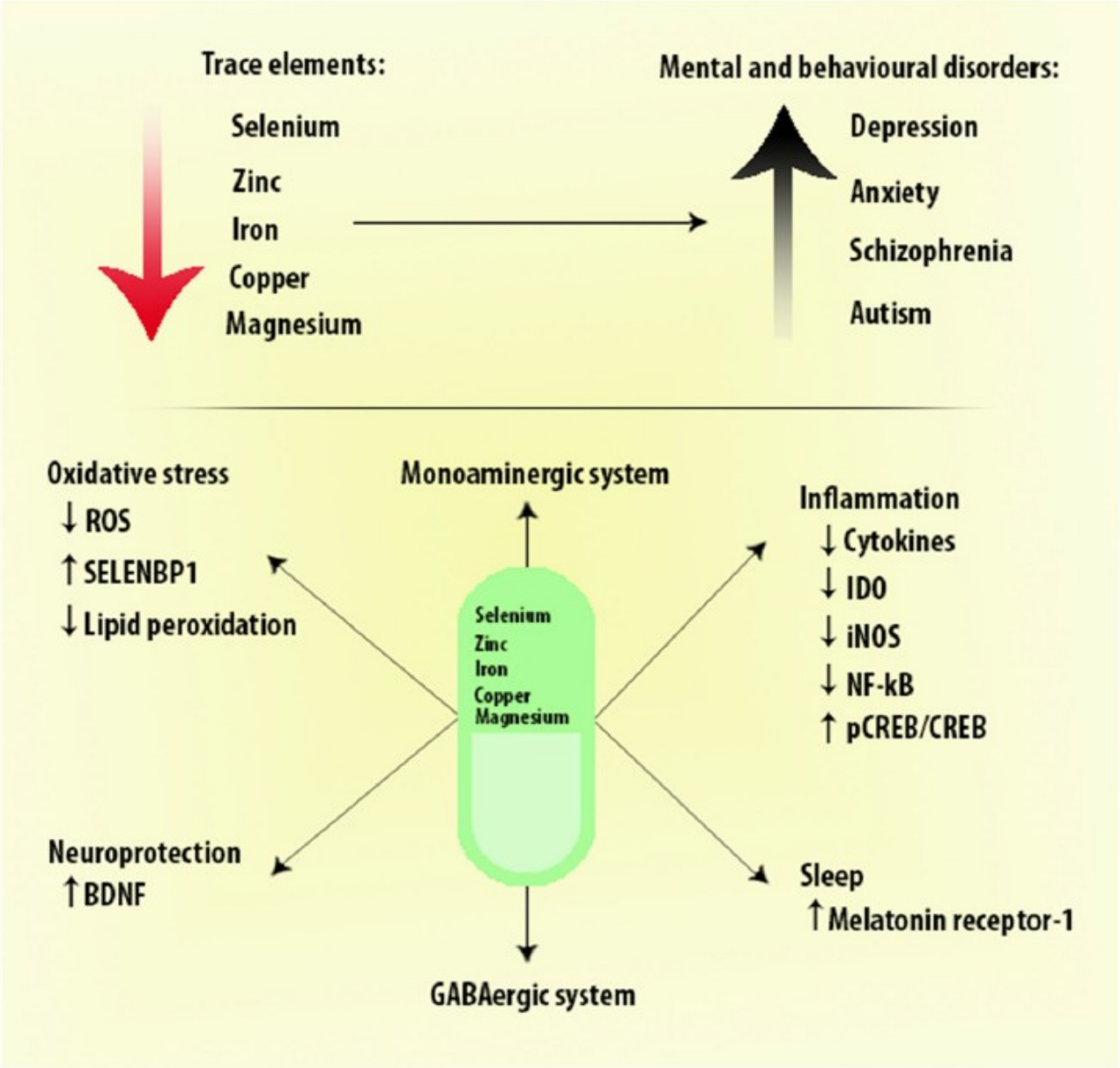
Dominika Głąbska [1,*], Aleksandra Kołota [1], Katarzyna Lachowicz [1], Dominika Skolmowska [1], Małgorzata Stachoń [1] and Dominika Guzek [2]

Table 10. The summary of observations and conclusions for the included studies of association between vitamin D and mental health, with the total Newcastle-Ottawa Scale (NOS) score.

Ref.	Potential Influence of Vitamin D	Results Supporting/Inconclusive/Not Supporting Positive Association between Vitamin D Intake and Mental Health *	Quality **
[37]	Reduced pain, fatigue, and depression, as well as improved upper-extremity function	Supporting	3
[41]	Reduced some behavioral problems	Supporting	5
[42]	Reduced depression	Supporting	4
[43]	Reduced externalizing behavior problems and attention deficit and improved cognition	Supporting	3
[44]	Reduced sleep disturbances	Supporting	4
[45]	Reduced depression and mania	Supporting	4
[46]	Reduced depression, irritability, tiredness, mood swings, sleep difficulties, weakness and pain, as well as improved well-being and ability to concentrate	Supporting	3
[47]	Reduced externalizing and internalizing problems	Supporting	7
[48]	Improved quality of life	Supporting	3
[49]	Reduced anxiety	Supporting	5
[50]	Reduced/not reduced depression (depending on analysis)	Inconclusive	4
[51]	No effect on bipolar disorder and major depressive disorder	Not supporting	2
[52]	No effect on obsessive compulsive disorder, but reduced obsession component	Inconclusive	4
[53]	Reduced obsessive compulsive disorder	Supporting	5
[54]	Reduced emotional problems and peer relationship problems	Supporting	5
[55]	No effect on mental health	Not supporting	5
[56]	Reduced depression	Supporting	3
[57]	Reduced distress and improved quality of life	Supporting	5
[58]	Reduced anger, anxiety, depression and worry, as well as improved quality of sleep	Supporting	5
[59]	Reduced depression	Supporting	4
[60]	Reduced/not reduced depression (depending on analysis)	Inconclusive	5
[61]	Reduced psychotic features	Supporting	5
[62]	Reduced prosocial problems	Supporting	8
[63]	In longer term reduced depression	Supporting	7

Glabska D, et al. Nutrients **2021**, 13, 952.

Ruhsal Bozukluklarda Eser Elementlerin Rolü



Shayganfard M. 2022

DEMİR

Eksikliği dünyada en yaygın beslenme bozukluğu

- Süt çocuklarında

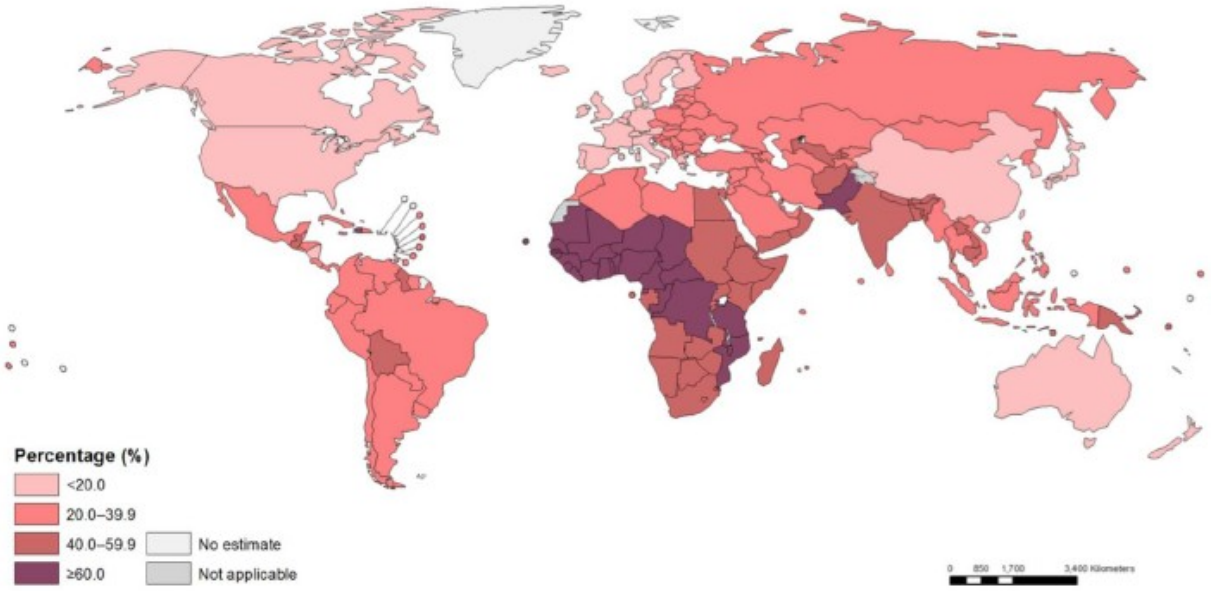
  6-10 mg/gün

- Çocuklarda

  10-15 mg/gün

  (RDA 1989)

Global estimates of the prevalence of anaemia in infants and children aged 6–59 months, 2011



Source: WHO. The global anaemia prevalence in 2011. Geneva: World Health Organization; 2015.

Demir Eksikliği Anemisi (DEA)

- WHO, Dünya'da 5 yaş altı , DEA prevalans %42.6,
  düşük gelir düzeyli ülkelerde %70 (*WHO 2021)*

- Türkiye'de DEA prevalans 6-59 ay çocuklarda %19.2 *(Erdoğan, 2019)*
  kız ergenlerde %15.9 *(Baykan, 2020)*

OPEN

017
ary 2018

Peripheral iron levels in children with attention-deficit hyperactivity disorder: a systematic review and meta-analysis

Ping-Tao Tseng[1,2], Yu-Shian Cheng[1], Cheng-Fang Yen[3,4], Yen-Wen Chen[5], Brendon Stubbs[6,7,8], Paul Whiteley[9], Andre F. Carvalho[10], Dian-Jeng Li[11,12], Tien-Yu Chen[13], Wei-Cheng Yang[14], Chia-Hung Tang[15], Che-Sheng Chu[16,17], Wei-Chieh Yang[18], Hsin-Yi Liang[19], Ching-Kuan Wu[1] & Pao-Yen Lin[20,21]

There is growing recognition that the risk of attention-deficit hyperactivity disorder (ADHD) in children may be influenced by micronutrient deficiencies, including iron. We conducted this meta-analysis to examine the association between ADHD and iron levels/iron deficiency (ID). We searched for the databases of the PubMed, ScienceDirect, Cochrane CENTRAL, and ClinicalTrials.gov up to August 9th, 2017. Primary outcomes were differences in peripheral iron levels in children with ADHD versus healthy controls (HCs) and the severity of ADHD symptoms in children with/without ID (Hedges' g) and the pooled adjusted odds ratio (OR) of the association between ADHD and ID. Overall, seventeen articles met the inclusion criteria. Peripheral serum ferritin levels were significantly lower in ADHD children (children with ADHD = 1560, HCs = 4691, Hedges' $g = -0.246$, $p = 0.013$), but no significant difference in serum iron or transferrin levels. In addition, the severity of ADHD was significantly higher in the children with ID than those without ID (with ID = 79, without ID = 76, Hedges' $g = 0.888$, $p = 0.002$), and there was a significant association between ADHD and ID (OR = 1.636, $p = 0.031$). Our results suggest that ADHD is associated with lower serum ferritin levels and ID. Future longitudinal studies are required to confirm these associations and to elucidate potential mechanisms.

- 17 makale
- DEHB'de periferik demir seviyesinin kontrol grubunun karşılaştırılması
- Serum ferritin düzeyleri DEHB'li çocuklarda daha düşük (serum demir ve transferrin düzeyleri için geçerli değil)
- DEHB şiddeti, demir eksikliği olanlarda demir eksikliği olmayanlara göre daha şiddetli

Research article | Open Access | Published: 04 June 2013

Association between psychiatric disorders and iron deficiency anemia among children and adolescents: a nationwide population-based study

Mu-Hong Chen, Tung-Ping Su, Ying-Sheue Chen, Ju-Wei Hsu, Kai-Lin Huang, Wen-Han Chang, Tzeng-Ji Chen & Ya-Mei Bai

BMC Psychiatry **13**, Article number: 161 (2013) | Cite this article

- 1996-2008 kayıtlarından DEA, yaş cinsiyet eşleştirilmiş kontroller ile karşılaştırılmış ve psikiyatrik bozukluklar için risk artışı değerlendirilmiş,

- 2957 DEA'lı hasta
  - Unipolar depresyon OR:2.34
  - Bipolar bozukluk OR: 5.78
  - Anksiyete bozukluğu OR: 3.46
  - OSB OR:3.08
  - ADHD OR:1.70
  - Gelişim Geriliği OR: 2.45
  - Mental Retardasyon OR: 2.70

Table 3. Summary of clinical evidence for the relationship between iron (Fe) and anxiety.

Participants	Measures	Key Results	Authors and Year
Chilean children (infancy–adolescence)	Youth Self Report by adolescents and the Child Behavior Checklist by parents; blood Fe at 12 and 18 months	Greater self-reported anxiety symptoms during adolescence for participants with Fe deficiency as an infant	Doom et al., 2018 [69]
Taiwanese children and adolescents with IDA	National Health Insurance Database from 1996 to 2008 used to identify children and adolescents with IDA; coexisting anxiety disorders were determined by specific diagnostic codes	IDA correlated with an increased risk for anxiety disorder	Chen et al., 2013 [70]
Adolescent females	Psychiatric assessment to determine anxiety status; serum ferritin	Serum ferritin was inversely correlated with both anxiety and depressive symptom severity	Abbas et al., 2021 [71]
Turkish adults	Hospital Anxiety and Depression Scale; diagnosis of IDA	Patients with IDA had higher levels of anxiety compared to the control group	Semiz et al., 2015 [72]
Students from the University of Santo Tomas in Sampaloc, Manila	General Anxiety Disorder-7 questionnaire; symptom-based IDA questionnaire	Positive association between symptom-based IDA and anxiety for females but not for males	Buita et al., 2021 [73]
Male Japanese students	State-Trait Anxiety Inventory A-Trait scale; brief-type self-administered diet history questionnaire	Low dietary Fe intake was associated with poor sleep quality and poor sleep was associated with higher anxiety	Matsunaga et al., 2021 [74]
Elderly Canadians	General Well-Being Questionnaire; liquid nutritional supplement; serum Fe	Supplemented group had increased serum Fe and improved anxiety and general well-being scores	Krondl et al., 1999 [77]
Patients with inflammatory bowel disease and IDA	EuroQoL questionnaire to assess anxiety; one capsule/day for 12 weeks Sucrosomial® Fe supplement	Sucrosomial® Fe supplement improved anxiety symptoms	Bastida et al., 2021 [78]
Italian pregnant women with IDA	State-Trait Anxiety Inventory; one capsule/day for one year of Sideremil™ liposomal Fe pyrophosphate/ascorbic acid supplement	Fe supplementation reduced anxiety and increased key Fe-related proteins hemoglobin, ferritin, and transferrin	Vitale et al., 2022 [79]
South African anemic mothers	Edinburgh Postnatal Depression Scale and State-Trait Anxiety Inventory; 125 mg Fe sulfate supplements from 10 weeks of pregnancy to nine months postpartum; Fe status assessed using hemoglobin, mean corpuscular volume, and transferrin saturation	Fe status was inversely associated with stress and anxiety and Fe supplementation improved stress scores	Beard et al., 2005 [80]

ÇİNKO (ZN)

- Kognitif fonksiyon
- Anksiyete

- Melatonin metabolizması için gerekli, dopamin regülasyonunda etkili (dopamin reuptake inhibitörü olarak bahsedilir)

- Bu konuda yayınlar en çok kadın ve çocukları etkileyen iki ruh sağlığı sorununa işaret ediyor. Depresyon ve ADHD

ÇİNKO (ZN)

- Anti anksiyete etkisi söz konusu
- Anskiyete ve uyku bozukluklarında diyetle çinko alımı arasında ters korelasyon mevcut

[Relationship between serum zinc levels and attention deficit hyperactivity disorder in children].

2015 yılı meta-analizinde 17 çalışma
2177 DEHB, 2900 sağlıklı
Serum çinko seviyeleri DEHB'li bireylerde daha düşük (p:0.003)

Blood and hair zinc levels in children with attention deficit hyperactivity disorder: A meta-analysis

Jiamei Luo [1], Yunbo Mo [1], Min Liu

Zinc status in attention-deficit/ hyperactivity disorder: a systematic review and meta-analysis of observational studies

Seyed Mojtaba Ghoreishy, Sara Ebrahimi Mousavi, Farzaneh Asoudeh &

2020 ve 2021 yılları meta-analizlerinde DEHB' de serum ve saçta çinko düzeylerinde DEHB'lilerde kontrol grubuna göre anlamlı farklılık bulunmamış

Reviews

The effect of zinc supplementation in children with attention deficit hyperactivity disorder: A systematic review and dose-response meta-analysis of randomized clinical trials

Sepide Talebi, Maryam Miraghajani, Abed Ghavami & Hamed Mohammadi

Pages 9093-9102 | Published online: 29 Jun 2021

6 RCT, 489 okul çağı çocuğu
Çinko desteği ile DEHB toplam skorunda kontrollere göre anlamlı azalma (p:0.04) varken dikkatsizlik (p:0.17) ve hiperaktivite (p:0.44) skorunda farklılık saptanmadı.
Kanıt kesinliği orta ile çok düşük arasında olarak belirlendi

Zinc intake, status and indices of cognitive function in adults and children: a systematic review and meta-analysis

- Çocuklarda 6 RCT ile yapılan metanaliz sonuçları:
- Çinko alımının billişsel işlevlerin herhangi bir alanında (zeka, yürütücü işlevler ve motor beceriler) bir etkisi olmadığını ortaya koymuş
- Çinko takviyesinin bilişssel işlevsellikte etkisini gösteremedi, ancak takviyeyi takiben yürütücü işlev ve motor gelişim yönünde bazı küçük iyileşme göstergeleri söz konusuydu

Warthon-Medina M, et al E J Clin Nutr. 2015

Çinko-Anksiyolitik Etki

Table 1. Summary of clinical evidence for the relationship between zinc (Zn) and anxiety.

Participants	Measures	Key Results	Authors and Year
Female high school students	Hospital Anxiety and Depression Scale; serum Zn	Inverse association between serum Zn and anxiety	Tahmasebi et al., 2017 [28]
Female university students	Beck Anxiety Inventory survey; dietary Zn assessment using a 12-month food frequency questionnaire	Inverse association between dietary Zn intake and anxiety	Hajianfar et al., 2021 [29]
Adult Japanese Workers	Kessler Psychological Distress Scale; dietary Zn assessed using three-month food frequency questionnaire	Inverse association between dietary Zn and anxiety symptoms	Nakamura et al., 2019 [30]
Children and adolescents with ADHD	Conners' Parent Rating Scale, Conners' Teacher Rating Scale; serum Zn	Low serum Zn correlates with higher anxiety and conduct issues	Oner et al., 2010 [32]
Male Chinese individuals	Self-Rating Anxiety Scale; cerebrospinal fluid Zn concentration	Cerebrospinal fluid Zn was negatively correlated with anxiety symptoms	Song et al., 2016 [33]
Adults from Bangladesh with generalized anxiety disorder	Patients previously diagnosed with generalized anxiety disorder were recruited; serum Zn	Participants with anxiety had low serum concentrations of Zn	Islam et al., 2013 [34]
Patients with CHD and T2DM	Beck Anxiety Inventory; serum Zn	Zn sulfate and magnesium oxide supplementation reduced anxiety symptoms.	Hamedifard at al., 2020 [35]
Iranian Females	Premenstrual Symptoms Screening Tool-Adolescent questionnaire; 220 mg/day elemental zinc supplement for 24 weeks	Zn supplementation reduced anxiety and other symptoms related to PMS	Ahmadi et al., 2022 [36]

Magnezyum

- Sinir iletimi ve nöromuskuler iletimde esas rol
- Eksitotoksisiteye (nöronal hücre ölümü) karşı koruyucu rolü vardır

Magnezyum Zengini Gıdalar

Low dietary intake of magnesium is associated with increased externalising behaviours in adolescents

Lucinda J Black[1,*], Karina L Allen[1,2], Peter Jacoby[1], Gina S Trapp[1], Caroline M Gallagher[1], Susan M Byrne[2] and Wendy H Oddy[1]

Table 2 General linear mixed model coefficients for YSR T-scores and zinc and magnesium intakes at ages 14 and 17 years, Western Australian Pregnancy Cohort (Raine) Study

	Zn			Mg		
	*β**	95 % CI	*P*	*β**	95 % CI	*P*
Unadjusted						
Total	0·35	−0·25, 0·96	0·256	0·31	0·16, 0·80	0·191
Internalising	0·09	−0·58, 0·76	0·796	0·01	−0·51, 0·54	0·961
Externalising	0·35	−0·28, 0·98	0·273	0·39	−0·11, 0·89	0·126
Adjusted†						
Total	−0·48	−1·29, 0·32	0·241	−0·44	−1·35, 0·47	0·342
Internalising	−0·07	−0·97, 0·84	0·887	0·52	−0·50, 1·53	0·316
Externalising	−0·73	−1·57, 0·10	0·085	−1·45	−2·40, −0·50	0·003

YSR, Youth Self-Report.
*Estimated difference in YSR T-scores per SD increase in Zn and Mg intakes.
†Adjusted for sex, physical activity, family income, supplement status, dietary misreporting, BMI, family functioning and energy intake; *n* 667 at 14 years, *n* 607 at 17 years.

Significantly lower serum and hair magnesium levels in children with attention deficit hyperactivity disorder than controls: A systematic review and meta-analysis

- 12 çalışmadan oluşan bir metanaliz
- Periferik kan Mg düzeyleri (plasma, serum ya da tam kan) DEHB tanılı çocuklarda kontrollerden daha düşük
- Sub-grup analizlerinde de serum MG düzeyleri, saç Mg seviyeleri DEHB tanılı çocuklarda kontrollerden düşük

Huang YH, et al. Progress in Neuro-Psychopharmavology and Biological Psychiatry, 2019

L-Threonic Acid Magnesium Salt Supplementation in ADHD: An Open-Label Pilot Study

Craig Surman [1], Carrie Vaudreuil [1], Heidi Boland [1], Lauren Rhodewalt [1], Maura DiSalvo [1], Joseph Biederman [1]

Affiliations + expand

PMID: 32162987 DOI: 10.1080/19390211.2020.1731044

Abstract

Objective: Attention-deficit/hyperactivity disorder (ADHD) is estimated to affect up to 5% of adults worldwide. Preclinical work demonstrates that L-Threonic Acid Magnesium Salt (LTAMS) administration is associated with neurobiological and neurofunctional effects that could offer clinical benefits in ADHD treatment.**Methods:** Participants were 15 adults with ADHD of moderate severity. Subjects received up to 12 weeks of open-label LTAMS administered as MMFS302 and MMFS202. The study was approved by the Institutional Review Board and posted on ClinicalTrails.Gov (NCT02558790).**Results:** 47% of subjects met our criteria of response attaining a CGI-Improvement score ≤2 and AISRS total reduction ≥25%. Significant improvement was seen in the AISRS, CGI-I, and the shifting subscale of the BRIEF. Changes in IQ and WASI-II performance were favorable and significant in the study population.**Conclusion:** LTAMS supplementation was found to be effective and well tolerated. Nearly half of participants met our definition of ADHD symptom clinical response. These results support the need to further evaluate this compound in larger samples under double-blind conditions.

The Role and the Effect of Magnesium in Mental Disorders: A Systematic Review

Andrea Botturi [1,*,†], Valentina Ciappolino [2,†], Giuseppe Delvecchio [3], Andrea Boscutti [2], Bianca Viscardi [2] and Paolo Brambilla [2,3]

- 18 makale depresif bozukluk
- 4 makale Anksiyete Bozukluğu
- 4 makale DEHB
- 3 makale OSB
- 1 makale OKB
- 1 makale SCH
- 1 makale YB

- 12 çalışma depresif belirtilerde azalma bildirmiştir
- 7 çalışma düşük magnezyum düzeyleri ve depresif psikometrik ölçek puanları arasında anlamlı korelasyon
- 2 makale magnezyım alımından sonra depresif semptomlarda azalma
- 2 makalede magneziyum düzeyleri ve anksiyete bozuklukları arasında ilişki bulunmadı
- 2 makalede DEHB ile ilişkili düşük magnezyum seviyeler
- 1 makalede ASD ile ilişkili düşük magnezyum seviyeleri

Botturi A, et al. Nutrients 2020

Selenyum

- Selenyum glutatyon peroksidaz kofaktörü, selonoproteinlerle ilişkili
- Serbest radikallerin ürettiği hücre hasarını önleyen güçlü antioksidan

Selenyum

Lower serum selenium concentration associated with anxiety in children

Jill Portnoy [a], Jessica Wang [b], Fenfen Wang [b], Phoebe Um [c], Sharon Y. Irving [b], Laura Hackl [d], Jianghong Liu [b]

- 831 çocuk (yaş:12.6 %46.1 kız)
- SCARED

- Karşıtırıcı faktörler kontrol edildiğinde, düşük selenyum konsantrasyonları
  - Total anksiyete (OR:0.992 $p < 0.01$)
  - Panic/somatic disorder (OR = 0.993, $p < 0.05$),
  - Generalized anxiety disorder (OR = 0.990, $p < 0.05$),
  - Social anxiety disorder (OR = 0.991, $p < 0.01$),
  - School phobia (OR = 0.989, $p < 0.01$),
  - but not separation anxiety (OR = 1.000, $p > 0.05$).

- Düşük selenyum konsantrasyonları ayrıca daha yüksek sürekli toplam kaygı, yaygın anksiyete ve okul fobisi puanları ile ilişkilendirildi. ($p<0,05$)

Portnoy J, et al. J pediatr Nurs 2022

Selenium status during pregnancy and child psychomotor development–Polish Mother and Child Cohort study

Kinga Polanska [1], Anna Krol [1], Wojciech Sobala [1], Jolanta Gromadzinska [2], Renata Brodzka [2], Gemma Calamandrei [3], Flavia Chiarotti [3], Wojciech Wasowicz [2], Wojciech Hanke [1]

- 410 anne-çocuk
- Se düzeyleri her trimersterda, doğumda ve kord kanında ölçülüyor
- Psikomotor gelişim 1 yaş ve 2 yaşta Bayley ile değerlendirilmiş
- İlk trimesterda Se düzeyi ile 1 yaş motor gelişim ve 2 yaş dil gelişimi arasında anlamlı pozitif ilişki
- 2 yaş kognitif skorlarda sınırda anlamlı pozitif etki (p:0.05) saptanmış

Polanska K, Pediatr Res. 2016

İlaç kullanımına bağlı vitamin eksiklikleri

- Mineral yağlar: A vitamini
- Kolestiramin: D, E, K vitamini, folik asit
- Antikonvülzanlar (fenitoin, fenobarbital, karbamezapin): D vit.
- Antibiyotikler: K vitamini
- Loop diüretikleri: B1 vitamini
- Proton pompa inhibitörleri, antiasitler: B12 vitamini
- İzoniazid: Niasin, piridoksin
- Metotreksat, sulfasalazin: Folik asit

Vitamin mineral eksikliği için riskli, destekten yararlanabilen çocuk ve adölesanlar

- İştahsızlık, anoreksiya
- Seçici beslenme
- Yetersiz süt ve süt ürünü tüketimi
- Sosyo ekonomik riskli grup, ihmal ve istismar
- Obezite tedavisi
- Düşük tartılı çocuklar

Table 3 Studies that investigated the effects of essential trace elements on depression

Trace element	Model	Findings	Publish year	Ref
Selenium	In vivo	Selenium decreased depression-like behavior, corticosterone and oxidative stress markers, inhibited stress-induced downregulated glucocorticoid receptor and BDNF mRNA levels, increased expression of NF-kB, iNOS, TNF-α, indoelamine-2,3-dioxygenase, and glycogen synthase kinase-3β	2019	[221]
Selenium	Human	Low dietary intake of selenium increased depressive symptoms	2019	[222]
Selenium	In vivo	Selenium decreased the depression-like behavior and cognitive impairment, the levels of reactive species, nitrite, lipid peroxidation and acetylcholinesterase activity	2019	[223]
Selenium	Human	No relationship between selenium levels and the risk of postnatal depression	2020	[224]
Zinc	Human	Lower serum zinc levels led to neuronal deficits and alterations of neuronal biochemical metabolite ratios	2020	[226]
Zinc	In vivo	Zinc increased BDNF and the ratio of pCREB/CREB protein levels, supplementation of imipramine led to an elevation in Zinc levels	2020	[225]
Zinc	Human	Zinc decreased the immune-inflammatory reaction	2020	[227]
Zinc	In vivo	Lower levels of zinc were related to depressive-like behavior	2020	[228]
Zinc	In vivo	Zinc increased the antidepressant and locomotor impact of clomipramine and prevented the oxidative stress	2019	[229]
Zinc	Human	Dietary zinc decreased the score of depression	2018	[230]
Magnesium	Human	The consumption of dietary magnesium led to the decreased risk of depression.	2019	[231]
Magnesium	Human	Lower serum magnesium concentrations led to depression	2019	[232]
Magnesium	Human	Dietary treatment with magnesium decreased stress in healthy adults with low magnesemia	2018	[233]
Magnesium	Human	Increased dietary intake of magnesium was related to decreased anxiety odds, inadequate intake of magnesium was correlated with anxiety	2018	[234]
Copper	In vivo	Memantine suppressed copper levels and improved depression behavior	2020	[235]
Copper	Human	Reduced depressive symptoms were related to higher circulating copper levels. Copper was also strongly correlated with the levels of BDNF	2019	[236]
Copper	Human	Sertraline treatment remarkably decreased copper levels	2019	[227]
Copper	Human	Increased serum copper concentrations led to neuronal dysfunction by influencing the neuronal biochemical metabolite ratios of major depressive disorder	2020	[226]
Copper	Human	Higher RBC AChE, and plasma PON1 as well as copper concentrations in people with moderate depression	2020	[237]
Copper	Human	Lower depression symptoms and BDNF levels were associated with higher copper levels	2020	[236]
Iron	Human	Iron deposits in the thalamus led to depressive symptoms	2019	[238]
Iron	Human	Lower cord blood ferritin and hemoglobin led to higher maternal prenatal psychosocial stress and pregnancy	2020	[239]
Iron	Human	No associations between psychosocial stress in infants and iron deficiency	2019	[240]
Iron	Human	Higher levels of depression during pregnancy was correlated to the iron deficiency	2018	[241]
Iron	Human	Depressed mood, functional fatigue and lower memory ability was correlated with lower iron status.	2020	[243]
Iron	Human	Inadequate iron status was strongly associated with depression	2019	[244]
Iron	Human	Ferritin deficiency led to aggravation of depressive symptoms and a reduction in quality of life.	2020	[245]

Table 2 Studies that investigated the effects of essential trace elements on anxiety

Trace element	Model	Findings	Publish year	Ref
Selenium	In vivo	Selenium increased ARS-induced anxiety-like behaviors, decreased the expressions of pro-inflammatory cytokines, IDO and iNOS, downregulated NF-kB, increased BDNF, decreased ROS generation and lipid peroxidation, decreased corticosterone levels	2019	[216]
Selenium	In vivo	Selenium increased the behavioral impairments, decreased the expression of pro-inflammatory cytokines and IDO in the prefrontal cortex and hippocampus	2019	[215]
Selenium	Human (adolescents)	Low selenium concentrations increased the development of anxiety	2020	[217]
Zinc	Human (adolescents)	Low dietary zinc intake decreased anxiety and sleep disorder	2020	[218]
Zinc gluconate/zinc sulfate	In vivo	Zinc sulfate had a neuroprotective effect, zinc gluconate had an anxiolytic effect	2020	[219]
Zinc	Human (elderly population)	Dietary zinc were not correlated with anxiety	2020	[220]

Table 4 Studies that investigated the effects of essential trace elements on autism

Trace element	Model	Findings	Publish year	Ref
Selenium	Human	The low levels of serum and toenail selenium led to increased autism existence	2020	[255]
Selenium	Human	Increased Hg and Pb and decreased selenium concentrations in autistic patients	2017	[256]
Zinc	In vivo	Zinc helped rescue the synaptic expression of proteins regulated by CTTNBP2 and increased social activity	2020	[259]
Zinc	In vivo	Dietary zinc supplementation inhibited repeated and anxiety-related autism-related activities and deficiencies in the recognition of social novelty, increased the recruitment to synapses of zinc-sensitive SHANK2, decreased synaptic transmission	2018	[260]
Zinc	In vivo	Maternal zinc diet decreased autism-related social interaction deficiencies and normalized anxiety behaviors.	2020	[261]
Zinc	Human	Low salivary zinc concentration in autism patients	2019	[262]
Zinc	Human	Zinc supplementation increased genetic expression of MT-1	2019	[263]
Zinc	In vivo	Zinc has role in developing brain lateralization	2018	[264]
Magnesium	Human	Neonatal magnesium concentrations were not correlated with a lowered risk of autism	2018	[265]
Magnesium	Human	No difference of magnesium levels in ADHD and autism	2020	[266]
Iron	Human	Children with autism had lower amounts of hemoglobin, hematocrit, iron, and MCV, lower concentrations of hemoglobin, hematocrit, and MCV in preschool autism patients, lower hemoglobin and hematocrit concentrations in autism patients with intellectual disability. lower level of hemoglobin in patients with severe autism	2017	[267]
Iron	Human	The brain iron content of preschool children with autism is lower than healthy ones	2020	[268]
Ferrous sulfate	Human	No significant effect on insomnia	2020	[269]

"Let Food be Thy Medicine"

Hippocrates